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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/556,641	11/06/2006	Sandrine Salle	REGIM 3.3-069	8511

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EXAMINER

WESTERBERG, NISSA M

ART UNIT	PAPER NUMBER
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1618

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04/13/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/556,641	Applicant(s) SALLE ET AL.	
	Examiner Nissa M. Westerberg	Art Unit 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 February 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 4, 5, 7 and 8 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 4, 5, 7, 8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>2/3/10</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicants' arguments, filed February 3, 2010, have been fully considered but they are not deemed to be fully persuasive. The following rejections and/or objections constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112 – 1st Paragraph

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 4, 5, 7 and 8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection. None of the water-insoluble acrylic polymer derivatives other than acrylic acid-methacrylic acid copolymers meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information for what they are and chemical structures are highly variant and encompass a myriad of possibilities. The specification provides insufficient written description to support the genus of derivatives of water-insoluble acrylic acid polymers encompassed by the claim, since there is no

description of the structural relationship of these derivatives provided in the specification and Applicant has not provided a description as to how the base molecule may be changed while remaining a derivative.

Claim Rejections - 35 USC § 112 – 2nd Paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1 and 4, 5, 7 and 8 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is MAINTAINED for the reasons of record set forth in Office Action mailed August 3, 2009 and those set forth below.

Applicant traverses this rejection on the grounds that "softening point" is an established technical term that is widely used in the fields of oils and waxes. Measurement of the softening point is known in the art, as shown by the enclosed ASTM D6090 reference. One of ordinary skill would understand what is meant by the term "softening point".

These arguments are unpersuasive. Under the "Significance and Use" section of the submitted information regarding the ASTM D6090 test, it states that "softening does not take place at a definite temperature... [f]or this reason, the determination of the softening point must be made by a fixed, arbitrary, and closely defined method if the

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results obtained are to be comparable.” ASTM D6090 is one such closely defined method that can be used to measure and compare softening points. While “softening point” may be a term used in the art, the field acknowledges that for values obtained to be compared, a “fixed, arbitrary and closely defined method” must be used. Applicants have not set forth a methodology by which the softening point of the materials encompassed by the claims is determined so that the softening points can be compared. Therefore, the claim is indefinite because the methodology used to determine this somewhat ambiguous value has not been set forth so an artisan could determine if a particular hot-melt low-melting substance falls within the limitation set forth by the claims or not.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

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4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).
9. Claims 1, 4, 5, 7 and 8 were rejected under 35 U.S.C. 103(a) as being unpatentable over Hara et al. (JP 02225416) in view of Samejima et al. (US 5,068,112) and Gowan, Jr. et al. (US 5,405,617). This rejection is MAINTAINED for the reasons of record set forth in the Office Actions mailed September 11, 2008, February 20, 2009 and August 3, 2009 and those set forth below.

Applicant traverses this rejection on the grounds that Hara does not disclose the pH-independent release of BPS or the use of the water-insoluble acrylic polymer derivatives of the claimed invention. The examples of enteric coating materials are all pH-dependent polymers which if used alone or in combination with the other disclosed water-soluble materials does not provide for pH-independent release. Comparative Example 2 shows that when water-insoluble materials such as those disclosed in Hara are combined with an API having a pH-dependent solubility (beraprost is one such

ingredient), the formulation exhibits a pH-dependent release of API. There is no disclosure that such a property is even desirable. Neither Samejima nor Gowan cure these deficiencies. Samejima applied a porous film coating of either a hydrophobic polymeric substance or a combination of hydrophobic and hydrophilic polymeric substances. The porosity of the different coatings results in different release rates but cannot provide sustained release of an API having a pH-dependent solubility. Samejima provides no disclosure of how to pick combinations of polymers that will result in pH-independent release. Gowan does not disclose that any of the hot-melt base materials can be selected to alter the drug release profile, let alone provide sustained release of BPS as claimed. There is also no disclosure in Gowan that the taste-masking hot-melt material could allow for pH-independent release. It is not sufficient that certain elements can be combined, but there must be some reason that they would be combined. Nothing in the combined teachings of the cited art lead to the conclusion that the films of Samejima or materials of Gowan would be combined with the Hara formulation to provide for a sustained release of BPS.

These arguments are unpersuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., pH-independent release of the active ingredient) are not recited in the rejected claim(s) 1, 4, 5 and 7. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The comparative example cited by Applicant set forth in the specification utilizes a single layer of a material (EUDRAGIT® RS) that was not disclosed by Hara. Applicants have not presented persuasive evidence that these pH-sensitive enteric, acrylic acid polymers in combination with a second skin layer as taught by the secondary references do not provide pH-independent release of the active ingredient with pH-sensitive solubility beraprost as required only by claim 8. Arguments without factual support are mere allegations and are not found to be persuasive.

In regards to Hara, there is a disclosure that either enteric coating or non-water soluble substances such as ethyl cellulose can be coated onto the beraprost granules (e.g., p 6, ¶ 3, and p 7, ¶ 4 of the translation). “Water-insoluble acrylic derivatives” is only one element in the Markush group of the first skin layer and Hara teaches ethyl cellulose, another member of that Markush group. It is noted that the acrylic acid enteric coating materials of Hara et al. still read on the instant limitation of “water insoluble acrylic polymer derivatives” as these materials are insoluble in water at the low pH values of the stomach.

In response to applicant's argument that the prior art does not appreciate that particular combinations coatings results in pH-independent sustained release of an active agent with a pH-dependent solubility, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). “[T]he discovery of a previously unappreciated property of a prior art composition, or of a

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scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). As set forth previously, the reason to combine the references is to provide a beraprost granule formulation with improved bioavailability from the enteric or non-water soluble coating (Hara) with an additional coating to taste mask the composition (Gowan, Jr. et al.; e.g. p 9 of the September 11, 2008 Office Action). While the reasoning may be different from that used by Applicant, the resulting granules having the same ingredients and structure, and thus the combination of cited prior art renders the instant claims obvious.

10. Claims 1, 4, 5, 7 and 8 were rejected under 35 U.S.C. 103(a) as being unpatentable over Hara et al. (JP 02225416) in view of Liversidge et al. (US 5,145,684) and Kokuno et al. (JP 01287021, 1989). This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed August 3, 2009 and those set forth below.

Applicant traverses this rejection on the grounds that there is no disclosure in Liversidge that modifying particle size would result in the sustained release of beraprost as in the instant invention or combining a water-insoluble acrylic polymer derivative with beraprost to provide the claimed release. Kukobu is directed towards a masking technique and does not disclose that these hot-melt base materials can be selected to

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alter the drug release profile of a formulation, let alone provide sustained of an API or pH-independent release of an API having pH-dependent solubility.

These arguments are unpersuasive. Hara et al. that discloses enteric coatings of methacrylic acid derived polymers or water-insoluble materials such as ethyl cellulose can be applied to prepare formulation with improved sustainability and bioavailability (p 7, last ¶). Only claim 8 required pH-independent release of beraprost sodium and Applicants have not provided evidence to establish that the compositions do not provide pH-independent release of beraprost sodium.

As discussed above, the reason for combining the prior art references set forth by the Examiner does not need be the same as the reasoning used by Applicant. That Applicants have appreciated that certain combinations of coatings allows for the pH-independent release of beraprost, an API with a pH-dependent solubility does not render the old composition patentably new to the discoverer.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8:00 a.m. - 4 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

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USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jake M. Vu/

Primary Examiner, Art Unit 1618

NMW